HEMISPHERX BIOPHARMA INC
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Registration No. 333-205228

PROSPECTUS SUPPLEMENT

(To Prospectus Dated August 4, 2015)

Up to $1,599,821

HEMISPHERX BIOPHARMA, INC.

Common Stock

This prospectus supplement and accompanying prospectus relates to the issuance and sale of up to $1,599,821 of our common stock, par value $0.001 per share, from time to time through our sales agent, Maxim Group LLC, or Maxim. These sales, if any, will be made under an equity distribution agreement, dated July 23, 2012, as amended, between us and Maxim, which we refer to as the Maxim Agreement.

Our common stock is listed on the NYSE American under the symbol “HEB.” The last reported sale price of our common stock on the NYSE American on November 24, 2017 was $0.32 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method permitted by law deemed to be an “at-the-market” offering as defined in Rule 415 under the Securities Act of 1933, as amended, which we refer to as the Securities Act. Maxim will act as sales agent on a commercially reasonable efforts basis, consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the NYSE American. There is no specific date on which the offering will end and there are no minimum sale requirements. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Maxim will be entitled to compensation at a fixed commission rate of 3.0% of the gross proceeds from the sale of common stock on our behalf pursuant to the Maxim Agreement. In connection with the sale of common stock on our behalf, Maxim will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Maxim will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Maxim with respect to certain liabilities, including liabilities under the Securities Act or under the

Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act.

As of November 27, 2017, the aggregate market value of our outstanding common stock held by non-affiliates was approximately $11,549,462 based on 31,866,347 shares of outstanding common stock, less approximately N51,586 shares held by affiliates, and a price of $0.37 per share, which was the last reported sale price of our common stock on the NYSE American on October 13, 2017. Pursuant to General Instruction I.B.6 of Form S-3, in no event during the period of twelve calendar months immediately prior to, and including, the date of any sales under this prospectus supplement, will we sell our common stock in a public primary offering with a value exceeding more than one-third of the aggregate market value of the common stock held by non-affiliates so long as our non-affiliate public float remains below $75 million. We have offered and sold $2,250,000 of securities pursuant to General Instruction I.B.6 of Form S-3 during the twelve calendar months prior to the date of this prospectus supplement.

You should read "Risk Factors" beginning on page S-6 of this prospectus supplement and the risk factors described in other documents incorporated by reference herein before buying our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement and the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Maxim Group LLC

The date of this prospectus supplement is November 27, 2017.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process and consists of two parts. The first part is this prospectus supplement, which describes the specific terms of this offering. The second part, the accompanying prospectus, gives more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated into each by reference include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents we have referred you to in the sections of this prospectus supplement and the accompanying prospectus entitled "Where You Can Find More Information; Information Incorporated By Reference."

You should rely only on this prospectus supplement, the accompanying prospectus, the information incorporated or deemed to be incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by us or on our behalf. We have not, and the sales agent has not, authorized anyone to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. We and the sales agent are not offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus or any free writing prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

All references in this prospectus supplement or the accompanying prospectus to "Hemispherx," the "Company," "we," "us," or "our" mean Hemispherx Biopharma, Inc., unless we state otherwise or the context otherwise requires.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that

jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. The summary may not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including "Risk Factors" and the financial statements and other information" contained in this prospectus supplement and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment in our common stock. This prospectus supplement may add to, update or change information in the accompanying prospectus.

Our Business

We are a specialty pharmaceutical company headquartered in Philadelphia, Pennsylvania and engaged in the clinical development of new drug therapies based on natural immune system enhancing technologies for the treatment of viral and immune based disorders. We were first formed in 1966 and in the early 1970s were doing contract research for the National Institutes of Health. Since that time, we have established a strong foundation of laboratory, pre-clinical and clinical data with respect to the development of natural interferon and nucleic acids to enhance the natural antiviral defense system of the human body and to aid the development of therapeutic products for the treatment of certain chronic diseases.

Our flagship products include Alferon N Injection® and the experimental therapeutic Ampligen®. Alferon N Injection® is approved for a category of STD infection, and Ampligen® represents an experimental RNA being developed for globally important viral diseases and disorders of the immune system. Hemispherx' platform technology includes components for potential treatment of various severely debilitating and life threatening diseases.

Our Corporate Information

Our principal executive office to 860 N. Orange Avenue, Suite B, Orlando, FL 32801, and we are in process of moving our Finance and Administration office within the Philadelphia area. The telephone number for our executive office is (407) 271-8516 and for our Finance & Administration office is 215-988-0080. We maintain a website at "http://www.hemispherx.net". Information contained on our website is not considered to be a part of, nor incorporated by reference in, this prospectus.

Certain Financial Information

As of September 30, 2017, we had approximately $2,303,000 in cash, cash equivalents, restricted cash and shorthand long-term investments. This amount is unaudited and does not present all information necessary for an understanding of our financial condition as of September 30, 2017. Please see out quarterly report on Form 10-Q for the quarter ended September 30, 2017.

THE OFFERING

Common Stock offered by us:	Shares of common stock, $0.001 par value per share, having an aggregate offering price of up to $1,599,821.
Manner of Offering:	"At-the-market" offering that may be made from time to time through our agent, Maxim. See "Plan of Distribution" on page **S-10**.
Use of Proceeds:	We currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital and general and administrative purposes. See "Use of Proceeds".
Risk Factors:	This investment involves a high degree of risk. You should read the "Risk Factors" section of this prospectus supplement and in the documents included in or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of risks to consider before deciding to purchase shares of our common stock.
NYSE American trading symbol:	"HEB"

Unless we indicate otherwise, all information in this prospectus is based on 31,866,347 shares of common stock outstanding as of November 27, 2017 and excluded:

1,190,567 shares of our common stock issuable upon exercise of outstanding stock options under our 2009 Equity Incentive Plan as, at a weighted average exercise price of $0.40, with 5,163,467 shares remaining available for future grants under such plan; and

7,342,825 shares of our common stock issuable upon exercise of outstanding warrants at a weighted average price of $0.65.

RISK FACTORS

Investment in our common stock involves a high degree of risk. In addition to the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, you should carefully consider the risks described below and in the section entitled "Risk Factors" in our Annual Report on Form 10-K for our most recent fiscal year filed with the Securities and Exchange Commission, subsequent Quarterly Reports on Form 10-Q, and in other reports we file with the Securities and Exchange Commission that are incorporated by reference herein, before making an investment decision. The following risks are presented as of the date of this prospectus supplement and we expect that these will be updated from time to time in our periodic and current reports filed with the Securities and Exchange Commission, which will be incorporated herein by reference. Please refer to these subsequent reports for additional information relating to the risks associated with investing in our common stock.

The risks and uncertainties described therein and below could materially adversely affect our business, operating results and financial condition, as well as cause the value of our common stock to decline. You may lose all or part of your investment as a result. You should also refer to the other information contained in this prospectus supplement and the accompanying prospectus, or incorporated by reference, including our financial statements and the notes to those statements, and the information set forth under the caption "Special Note Regarding Forward-Looking Statements." Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks mentioned below. Forward-looking statements included in this prospectus supplement are based on information available to us on the date hereof, and all forward-looking statements in documents incorporated by reference are based on information available to us as of the date of such documents. We disclaim any intent to update any forward-looking statements. The risks described below and contained in our Annual Report on Form 10-K, Form 10-Q and in our other periodic reports are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Related to this Offering

We will have broad discretion in how we use the proceeds, and we may use the proceeds in ways in which you and other stockholders may disagree.

We plan to use the net proceeds from the offering towards activities listed in Use of Proceeds". Pending these uses, we intend to invest the net proceeds in investment grade, interest bearing securities. Our management will have broad discretion in the application of the proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our operating results or enhance the value of our common stock.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the prices per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the prices per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into shares of our common stock, in future transactions may be higher or lower than the prices per share paid by investors in this offering.

It is not possible to predict the aggregate proceeds resulting from sales made under the Maxim Agreement.

Subject to certain limitations in the Maxim Agreement and compliance with applicable law, we have the discretion to deliver a placement notice to Maxim at any time throughout the term of the Maxim Agreement. The number of shares that are sold through Maxim after delivering a placement notice will fluctuate based on a number of factors, including the market price of our common stock during the sales period, the limits we set with Maxim in any applicable placement notice, and the demand for our common stock during the sales period. Because the price per share of each share sold will fluctuate during the sales period, it is not currently possible to predict the aggregate proceeds to be raised in connection with those sales.

The common stock offered hereby will be sold in "at-the-market" offerings, and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different levels of dilution and different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold in this offering. In addition, subject to the final determination by our board of directors, there is no minimum or maximum sales price for shares to be sold in this offering. Investors may experience a decline in the value of the shares they purchase in this offering as a result of sales made at prices lower than the prices they paid.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements in this prospectus and in the other filings incorporated by reference herein, constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended which we refer to as the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements reflect our current views with respect to future events and are based on assumptions and are subject to risks, uncertainties and other important factors. We discuss many of these risks, uncertainties and other important factors in greater detail under the “Risk Factor” sections in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and in subsequent Quarterly Reports on Form 10-Q, as well as other filings we make with the SEC (collectively, our “SEC Filings”), all of which are incorporated by reference herein. As the foregoing risks could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements made by us, you should not place undue reliance on any such forward-looking statements.

Further, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read the risks, uncertainties and other important factors in our SEC Filings completely and with the understanding that our actual future results may be materially different from what we expect. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our business, results of operations and financial condition. Any forward-looking statement speaks only as of the date on which it is made and we undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which will arise. We cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. Any statements in this prospectus, and in the other filings incorporated by reference herein about our expectations, beliefs, plans, objectives, assumptions or future events or performance that are not historical facts are forward-looking statements. You can identify these forward-looking statements by the use of words or phrases such as “believe”, “may”, “could”, “will”, “estimate”, “continue”, “anticipate”, “intend”, “seek”, “plan”, “expect”, “
“would,” and similar expressions intended to identify forward-looking statements.

Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties inherent in our business including, without limitation: our ability to adequately fund our projects as we will need additional funding to proceed with our objectives, the potential therapeutic effect of our products, the possibility of obtaining regulatory approval, our ability to find senior co-development partners with the capital and expertise needed to commercialize our products and to enter into arrangements with them on commercially reasonable terms, our ability to manufacture and sell any products, our ability to enter into arrangements with third party vendors, market acceptance of our products, our ability to earn a profit from sales or licenses of any drugs, our ability to discover new drugs in the future, changing market conditions, changes in laws and regulations affecting our industry, and issues related to our New Brunswick, New Jersey facility. We have disclosed that in

February 2013, we received a Complete Response from the U.S. Food and Drug Administration (the "FDA") declining to approve our Ampligen® New Drug Application ("NDA") for Chronic Fatigue Syndrome Treatment, sometimes referred to as myalgic encephalomyelitis/chronic fatigue syndrome ("ME/CFS"), stating that we should conduct at least one additional clinical trial, complete various nonclinical studies and perform a number of data analyses. Accordingly, the remaining steps to potentially gain FDA approval of the Ampligen® NDA, the final results of these and other ongoing activities could vary materially from our expectations and could adversely affect the chances for approval of the Ampligen® NDA. These activities and the ultimate outcomes are subject to a variety of risks and uncertainties, including but not limited to risks that (i) the FDA may ask for additional data, information or studies to be completed or provided; and (ii) the FDA may require additional work related to the commercial manufacturing process to be completed or may, in the course of the inspection of manufacturing facilities, identify issues to be resolved. With regard to our NDA for Ampligen® to treat ME/CFS, as noted above, there are additional steps which the FDA has advised Hemispherx to take in our seeking approval. The final results of these and other ongoing activities, and of the FDA review, could vary materially from Hemispherx' expectations and could adversely affect the chances for approval of the Ampligen® NDA. Any failure to satisfy the FDA's requirements could significantly delay, or preclude outright, approval of our drugs for commercial sale in the United States.

We also have disclosed that, in August 2016, we received approval of our NDA from Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica ("ANMAT") for commercial sale of rintatolimod (U.S. tradename: Ampligen®) in the Argentine Republic for the treatment of severe ME/CFS. The product will be marketed by GP Pharm, our commercial partner in Latin America. We believe, but cannot assure, that this approval provides a platform for potential commercial sales in certain countries within the European Union under regulations that support cross-border pharmaceutical sales of licensed drugs. In Europe, approval in a country with a stringent regulatory process in place, such as Argentina, should add further validation for the product as the Early Access Program as discussed below and underway in Europe in pancreatic cancer. ANMAT approval is only an initial, but important, step in the overall successful commercialization of our product. There are a number of actions that must occur before we could be able to commence commercial sales in Argentina. Commercialization in Argentina will require, among other things, an appropriate reimbursement level, appropriate marketing strategies, completion of manufacturing preparations for launch (including possible requirements for approval of final manufacturing) and we will need additional funds to manufacture product at a sufficient level for a commercial launch. There are no assurances as to whether or when such multiple subsequent steps will be successfully performed to result in an overall successful commercialization and product launch. Approval of rintatolimod for ME/CFS in the Argentine Republic does not in any way suggest that the Ampligen® NDA in the United States or any comparable application filed in the European Union or elsewhere will obtain commercial approval.

We also have disclosed that, in January 2017, the Early Access Program ("EAP") through our agreement with myTomorrows designed to enable access of Ampligen® to ME/CFS patients has been extended to pancreatic cancer patients beginning in the Netherlands. myTomorrows is our exclusive service provider in Europe and Turkey and will manage all EAP activities relating to the pancreatic cancer extension of the program. No assurance can be given that Ampligen® will prove effective in the treatment of pancreatic cancer.

In June 2017, we signed an amendment to the EAP with myTomorrows. This amendment is for MyTomorrows to provide support services to Hemispherx with respect to the execution of the 511-Program ("511-Services"). The 511-Services shall be rendered for a period of 6 months to be renewed with additional 6 month periods with written mutual consent, or until termination of the 511-Program. The 511-Services shall be rendered free of charge.

Our overall objectives include plans to continue seeking approval for commercialization of Ampligen® in the United States and abroad as well as seeking to broaden commercial therapeutic indications for Alferon N Injection® presently approved in the United States and Argentina. We continue to pursue senior co-development partners with the capital and expertise needed to commercialize our products and to enter into arrangements with them on commercially reasonable terms. Our ability to commercialize our products, widen commercial therapeutic indications of Alferon N Injection® and/or capitalize on our collaborations with research laboratories to examine our products are subject to a number of significant risks and uncertainties including, but not limited to our ability to enter into more definitive agreements with some of the research laboratories and others that we are collaborating with, to fund and conduct additional testing and studies, whether or not such testing is successful or requires additional testing and meets the requirements of the FDA and comparable foreign regulatory agencies. We do not know when, if ever, our products will be generally available for commercial sale for any indication.

We outsource certain components of our manufacturing, quality control, marketing and distribution while maintaining control over the entire process through our quality assurance and regulatory groups. We cannot provide any guarantee that the facility or our contract manufacturer will necessarily pass an FDA pre-approval inspection for Alferon® manufacture.

The production of new Alferon® API inventory will not commence until the validation phase is complete. While the facility is approved by FDA under the Biological License Application ("BLA") for Alferon®, this status will need to be reaffirmed by a successful Pre-Approval Inspection by the FDA prior to commercial sale of newly produced inventory product. If and when the Company obtains a reaffirmation of FDA BLA status and has begun production of new Alferon® API, it will need FDA approval as to the quality and stability of the final product to allow commercial sales to resume. We will need additional funds to finance the revalidation process in our facility to initiate commercial manufacturing, thereby readying ourselves for an FDA Pre-Approval Inspection. If we are unable to gain the necessary FDA approvals related to the manufacturing process and/or final product of new Alferon® inventory, our operations most likely will be materially and/or adversely affected. In light of these contingencies, there can be no assurances that the approved Alferon N Injection® product will be returned to production on a timely basis, if at all, or that if and when it is again made commercially available, it will return to prior sales levels.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to $1,599,821 from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares of our common stock under or fully utilize the Maxim Agreement as a source of financing.

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered by this prospectus. We currently intend to use the net proceeds from the sale of the securities offered by us hereunder, if any, for working capital and general and administrative purposes. Pending these uses, we plan to invest these net proceeds in short-term, interest bearing obligations, certificates of deposit or direct or guaranteed obligations of the United States.

PRICE RANGE OF OUR COMMON STOCK

The following table sets forth the high and low prices for our common stock for the last two fiscal years, the first two quarters of 2017 and the current quarter to date as reported by the NYSE American. The following prices give retroactive effect to the 12-to-1 reverse stock split effected on August 26, 2016.

	High	Low
COMMON STOCK		
Time Period:		
January 1, 2017 through March 31, 2017	$0.93	$0.39
April 1, 2017 through June 30, 2017	$0.84	$0.45
July 1, 2017 through September 30, 2017	$0.74	$0.30
October 1, 2017 through November 24, 2017	$0.37	$0.30
January 1, 2016 through March 31, 2016	$2.40	$0.78
April 1, 2016 through June 30, 2016	$1.92	$1.24
July 1, 2016 through September 30, 2016	$2.64	$1.24
October 1, 2016 through December 31, 2016	$1.26	$0.65
January 1, 2015 through March 31, 2015	$3.96	$2.52
April 1, 2015 through June 30, 2015	$3.48	$2.40
July 1, 2015 through September 30, 2015	$2.52	$1.68
October 1, 2015 through December 31, 2015	$2.16	$0.72

On November 24, 2017, the last sale price for our common stock on the NYSE American was $0.32 per share and there were approximately 87 holders of record of our common stock. This does not include the number of persons whose stock is in nominee or “street name” accounts through brokers.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock. We currently intend to retain any future earnings to finance the growth and development of our business. Therefore, we do not anticipate that we will declare or pay any cash dividends on our common stock in the foreseeable future. Any future determination to pay cash dividends will be at the discretion of our Board of Directors and will depend on our financial condition, results of operations, capital requirements, restrictions under any existing indebtedness and other factors the Board of Directors deems relevant.

CAPITALIZATION

The following table sets forth our consolidated cash and capitalization as of September 30, 2017. This table should be read in conjunction with our audited and unaudited financial statements incorporated by reference herein.

Cash and cash equivalents $2,303,000

Total indebtedness $3,666,000

Redeemable Warrants $1,018,000

Stockholders' equity:	
Preferred stock, par value $0.01 per share, authorized 5,000,000; issued and outstanding; none	—
Common stock, par value $0.001 per share, authorized 350,000,000 shares; issued and outstanding 31,077,372 and 24,202,921, respectively	31,000
Additional paid-in capital	316,748,000
Accumulated other comprehensive income	29,000
Accumulated deficit	(306,767,000)
Total stockholders' equity	10,041,000

PLAN OF DISTRIBUTION

We have entered into a sales agreement, dated July 23, 2012, as amended, with Maxim Group LLC ("Maxim"), under which we may offer and sell our common stock from time to time through Maxim, acting as our sales agent. Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus will be made at market prices by any method that is deemed to be an "at the market" offering as defined in Rule 415 under the Securities Act, including sales made directly on or through the NYSE American or any other trading market for our common stock.

Each time we wish to issue and sell our common stock under the Maxim Agreement, we will notify Maxim of the number of shares to be issued, the dates on which such sales are anticipated to be made, any minimum price below which sales may not be made and other sales parameters as we deem appropriate. Once we have so instructed Maxim, unless Maxim declines to accept the terms of the notice, and otherwise subject to the terms and conditions of the Maxim Agreement, Maxim will use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares of common stock up to the amount specified on such terms. The obligations of Maxim

under the Maxim Agreement to sell our shares of common stock is subject to a number of conditions that we must meet as specified in the Maxim Agreement.

We will pay Maxim a commission for its services in acting as agent in the sale of our common stock on our behalf under the Maxim Agreement. Maxim will be entitled to compensation at a fixed commission rate of 3.0% of the gross proceeds from the sale of common stock on our behalf pursuant to the Maxim Agreement. Because there is no minimum offering amount required as a condition to closing this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse Maxim for certain specified expenses, including the fees and disbursements of its legal counsel in connection with the preparation and execution of the Maxim Agreement and may in the future reimburse Maxim for additional out-of-pocket costs incurred by Maxim in connection with further due diligence of our company from time to time, including the fees and disbursements of Maxim's legal counsel.

We estimate that the total expenses for the offering set forth in this Prospectus Supplement, excluding compensation and reimbursements payable to Maxim under the terms of the Maxim Agreement, will be approximately $40,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of our common stock through Maxim under the Maxim Agreement.

Settlement for sales of our common stock will occur on the second trading day following the date on which any sales are made, or on some other date that is agreed upon by us and Maxim in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Maxim may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will report at least quarterly the number of shares of our Common Stock sold through Maxim under the Maxim Agreement, the net proceeds to us and the compensation paid by us to Maxim in connection with the sales of our common stock under the Maxim Agreement.

In connection with the sale of common stock on our behalf, Maxim will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Maxim will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Maxim against certain liabilities, including liabilities under the Securities Act or the Exchange Act.

The Maxim Agreement and an amendment thereto were filed as exhibits to our Current Reports on Form 8-K that we filed with the Securities and Exchange Commission in connection with this offering on July 23, 2012 and August 5, 2015, respectively, and are incorporated into this prospectus supplement by reference

Maxim and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

LEGAL MATTERS

The validity of the common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Silverman Shin & Byrne PLLC, New York, New York. Ellenoff Grossman & Schole LLP, New York, New York, is counsel for Maxim in connection with this offering.

EXPERTS

The financial statements incorporated in this prospectus supplement by reference from the Company’s Annual Report on Form 10-K have been audited by RSM LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference (which report expresses an unqualified opinion on the consolidated financial statements). Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC. This prospectus does not contain all of the information included in the registration statement. The registration statement that contains this prospectus supplement, including the exhibits to the registration statement, contains additional information about us and the securities offered by this prospectus supplement. For further information about us and our securities covered by this prospectus supplement and the accompanying prospectus, you should refer to the registration statement and the exhibits filed with the registration statement. We are subject to the information requirements of the Securities Exchange Act of 1934 and file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov or through our website at www.hemispherx.net. Information contained on our website is not considered to be a part of, nor incorporated by reference in, this prospectus. You may also read and copy any document we file with the SEC at its Public Reference Room at 100 F Street, NE, Washington, D.C. 20549.

You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Room of the SEC at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

IMPORTANT INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to "incorporate by reference" the information that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be an important part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the following documents and any future filing made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 prior to the termination of the offering:

The following documents previously filed by us with the SEC are incorporated by reference in this prospectus:

- Our Annual Report on Form 10-K for the year ended December 31, 2016, filed on March 31, 2017;
- Our quarterly reports on Form 10-Q for the quarters ended March 31, 2017, June 30, 2017 and September 30, 2017, filed on May 15, 2017, August 14, 2017 and November 14, 2017, respectively;
- Our Current Reports on Form 8-K filed with the Commission on January 17, 2017, February 1, 2017, February 3, 2017, April 3, 2017, June, 1, 2017, June 22, 2017, August 15, 2017, August 23, 2017, August 29, 2017 and September 14, 2017; and amended Current Report on Form 8-K/A filed with the Commission on May 8, 2017 Our definitive proxy statement on Schedule 14A filed on July 18, 2017; and
- A description of our common stock contained in our registration statement on Form S-1, SEC File No. 333-117178, filed on July 6, 2004, and any amendment or report filed for the purpose of updating this description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Investor Relations

One Penn Center, 1617 JFK Blvd., Suite 500

Philadelphia, PA 19103

Phone: 215-988-0080

Fax: 215-988-1739

Email: ir@hemispherx.net

You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized anyone else to provide you with different information. We will not make offers to sell these shares in any jurisdiction where the offer is not permitted.

PROSPECTUS

HEMISPHERX BIOPHARMA, INC.

$77,849,014

Debt Securities

Preferred Stock

Common Stock

Debt Warrants

Equity Warrants

Units

We may from time to time offer to sell any combination of debt securities, preferred stock, common stock, debt warrants, equity warrants and units described in this prospectus in one or more offerings. The aggregate initial offering price of all securities sold under this prospectus will not exceed $77,849,014.

This prospectus provides a general description of the securities we may offer. Each time we sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in any securities. This prospectus may not be used to consummate a sale of securities unless accompanied by the applicable prospectus supplement.

We will sell these securities directly to our stockholders or to purchasers or through agents on our behalf or through underwriters or dealers as designated from time to time. If any agents or underwriters are involved in the sale of any of these securities, the applicable prospectus supplement will provide the names of the agents or underwriters and any applicable fees, commissions or discounts.

Our common stock is traded on the NYSE MKT under the symbol “HEB.” On June 1, 2015, the last reported sale price for our common stock on the NYSE MKT was $0.23 per share. The aggregate market value of the outstanding shares of our common stock held by non-affiliates was $54,904,932, based on 242,554,673 shares of common stock outstanding, of which 238,717,096 are held by non-affiliates, and a closing sale price on NYSE MKT of $0.23 on June 1, 2015. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding more than one-third of our “public float” (the market value of our common stock held by our non-affiliates) in any 12-month period so long as our public float remains below $75,000,000. We have sold 16,677,755 shares of our common stock pursuant to General Instruction I.B.6. of Form S-3 during the twelve calendar months prior to and including the date of this prospectus.

Investing in our securities involves risks. See “Risk Factors“ on page 3.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is August 4, 2015

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission, or the Commission, utilizing a "shelf" registration process. Under this shelf registration process, we may offer to sell any combination of the securities described in this prospectus in one or more offerings up to a total dollar amount of $77,849,014. This prospectus provides you with a general description of the securities we may offer. Each time we sell securities under this shelf registration, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. To the extent that any statement that we make in a prospectus supplement is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. You should read both this prospectus and any prospectus supplement, including all documents incorporated herein or therein by reference, together with additional information described under "Where You Can Find More Information" and "Information Incorporated by Reference." We may only use this prospectus to sell the securities if it is accompanied by a prospectus supplement.

We have not authorized any dealer, salesman or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and the accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or the accompanying prospectus supplement. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and the accompanying prospectus supplement is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities are sold on a later date.

ABOUT HEMISPHERX

Hemispherx Biopharma, Inc. and its subsidiaries (collectively, "Hemispherx", "Company", "we" or "us") are a specialty pharmaceutical company headquartered in Philadelphia, Pennsylvania and engaged in the clinical development of new drug therapies based on natural immune system enhancing technologies for the treatment of viral and immune based disorders. We were founded in the early 1970s doing contract research for the National Institutes of Health. Since that time, we have established a strong foundation of laboratory, pre-clinical and clinical data with respect to the development of natural interferon and nucleic acids to enhance the natural antiviral defense system of the human body and to aid the development of therapeutic products for the treatment of certain chronic diseases. We have three domestic subsidiaries BioPro Corp., BioAegean Corp., and Core BioTech Corp., all of which are incorporated in Delaware and are dormant. Our foreign subsidiary is Hemispherx Biopharma Europe N.V./S.A. which was established

in Belgium in 1998.

Our flagship products include Alferon N Injection® and the experimental therapeutic Ampligen®. Alferon N Injection® is approved for a category of STD infection, and Ampligen® represents an experimental RNA being developed for globally important viral diseases and disorders of the immune system. Hemispherx' platform technology includes components for potential treatment of various severely debilitating and life threatening diseases. Alferon® LDO (Low Dose Oral) is a formulation under development targeting influenza. We own and operate a 43,000 sq. ft. FDA approved facility in New Brunswick, NJ.

Our principal executive offices are located at One Penn Center, 1617 JFK Boulevard, Suite 500, Philadelphia, Pennsylvania 19103, and our telephone number is 215-988-0080. We maintain a website at "http://www.hemispherx.net." Information contained on our website is not considered to be a part of, nor incorporated by reference in, this prospectus. Unless the context requires otherwise, references in this prospectus to "Hemispherx," the Company," "we," "us" and "our" refer to Hemispherx Biopharma, Inc.

RISK FACTORS

You should carefully consider the specific risks set forth under "Risk Factors" in the applicable prospectus supplement, under "Risk Factors" under Item 1A of Part I of our most recent annual report on Form 10-K, and under "Risk Factors" under Item 1A of Part II of our subsequent quarterly reports on Form 10-Q, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, or the Exchange Act, each of which is incorporated by reference in this prospectus, before making an investment decision. For more information, see "Information Incorporated by Reference."

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Any statements in this prospectus and the information incorporated herein by reference about our expectations, beliefs, plans, objectives, assumptions or future events or performance that are not historical facts are forward-looking statements. You can identify these forward-looking statements by the use of words or phrases such as “believe”, “may”, “could”, “will”, “estimate”, “continue”, “anticipate”, “intend”, “seek”, “plan”, “expect”, “should”, or “would”. Among the fact cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties inherent in our business including, without limitation: the potential therapeutic effect of our products, the possibility of obtaining regulatory approval, our ability to manufacture and sell any products, our ability to enter into arrangements with third party vendors, market acceptance or our products, our ability to earn a profit from sales or licenses of any drugs, our ability to discover new drugs in the future, changing market conditions, changes in laws and regulations affecting our industry, issues related to operations at of our New Brunswick, New Jersey facility; and other risks detailed in the documents incorporated by reference in this prospectus. If any of these risks or uncertainties materializes or any of these assumptions proves incorrect, our results could differ materially from the expectations in these statements. The forward-looking statements included in this prospectus are made only as of the date of this prospectus, and we are not under any obligation to update our respective forward-looking statements and do not intend to do so.

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement, we plan to allocate the net proceeds from the offering towards research and development, operations and general and administrative purposes related to the commercialization of Ampligen® and Alferon® related products, including, but not limited to, the following: (1) costs associated with validation of Alferon® production and preparation for the FDA pre-approval inspections of the facility, (2) manufacture of commercial product, (3) potential new preclinical and/or clinical studies in order to gain commercial approval for Ampligen® and broader approvals for Alferon® and Alferon LDO®, (4) working capital to build and maintain sufficient inventory by procuring raw materials, supplies and other items for the New Brunswick manufacturing facility, as well as to remunerate outside contractors for necessary services, such as, final filling and finishing operations in order to meet any anticipated demand from normal operations as well as through the possible pursuit of other disease areas and/or geographic regions that may present themselves, (5) potential establishment of sales and marketing capabilities, as well as consideration towards the expansion of our manufacturing capacity, and (6) working capital for general and administrative expenses. We will set forth in the particular prospectus supplement our intended use for the net proceeds we receive from the sale of our securities under such prospectus supplement. Pending the uses described above, we plan to invest the net proceeds of this offering in short and medium-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

RATIO OF EARNINGS TO FIXED CHARGES

The following summary is qualified by the more detailed information appearing in the computation table found in Exhibit 12.1 to the registration statement of which this prospectus is part and the historical financial statements, including the notes to those financial statements, incorporated by reference in this prospectus. Our ratio of earnings to fixed charges for each of the years ended December 31, 2010 to 2014 and the three months ended March 31, 2015 was as follows:

	Year Ended December 31,					Three Months Ended March 31, 2015
	2010	2011	2012	2013	2014	
Ratio of earnings to fixed charges(1)	—	—	—	—	—	—

(1) For purposes of computing this ratio of earnings to fixed charges, fixed charges consist of interest expense and premiums, discounts and capital expenses related to debt (loss) before income taxes plus fixed charges. Earnings were insufficient to cover fixed charges by approximately $13.1 million, $9.0 million, $17.3 million, $16.2 million and $17.5 million for the years ended December 31, 2010, 2011, 2012, 2013 and 2014 and $3.4 million for the first three months of 2015. We have not included a ratio of earnings to combined fixed charges and preferred stock dividends because we do not have any preferred stock outstanding as of the date of this prospectus.

We have incurred approximately $103,000 in fixed charges in the past five years. Fixed charges mainly represent interest expensed as well as amortized discounts related to indebtedness. We have incurred Net Losses totaling approximately $13.1 million, $9.0 million, $17.4 million, $16.2 million and $17.5 million for the years ended December 31, 2010, 2011, 2012, 2013 and 2014, respectively, and $3.4 million for the first three months of 2015. Until we achieve profitability, we will not be able to cover our fixed charges from earnings.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities separately or together:

through one or more underwriters or dealers in a public offering and sale by them;

through agents; and/or

directly to one or more purchasers.

We may distribute the securities from time to time in one or more transactions:

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

We may solicit directly offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time. We may sell the securities being offered by this prospectus by any method permitted by law, including sales deemed to be an “at the market” offering as defined in Rule 415(a)(4) of the Securities Act of 1933, as amended, or the Securities Act, including without limitation sales made directly on the NYSE MKT, on any other existing trading market for our securities or to or through a market maker. We will name in a prospectus supplement any agent involved in the offer or sale of our securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale and we will provide the name of any underwriter in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

We will provide in the applicable prospectus supplement any compensation we will pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

Unless otherwise specified in the prospectus supplement, each series of the securities will be a new issue with no established trading market, other than our common stock, which is currently listed on the NYSE MKT. We will apply to the NYSE MKT to list any additional shares of common stock that we offer and sell pursuant to a prospectus supplement. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involves the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with

any derivative transaction, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be identified in the applicable prospectus supplement or a post-effective amendment to the registration statement of which this prospectus is a part. In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the prospectus supplement the extent to which the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee to be identified in the applicable prospectus supplement. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement of which this prospectus forms a part and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, “Hemispherx,” “we,” “our” or “us” refer to Hemispherx Biopharma, Inc. excluding our subsidiaries, unless expressly stated or the context otherwise requires.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer’s certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the debt securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and

where notices and demands to us in respect of the debt securities may be delivered;

the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which debt securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;

the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;

the denominations in which the debt securities will be issued, if other than denominations of $1,000 and any integral multiple thereof;

whether the debt securities will be issued in the form of certificated debt securities or global debt securities;

the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;

the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;

the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;

if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies other than that in which the debt securities are denominated or designated to be payable or by reference to a commodity, commodity index, stock exchange index or financial index;

any provisions relating to any security provided for the debt securities;

any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;

any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;

any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;

the provisions, if any, relating to conversion or exchange of any securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange; and

any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in

a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depositary, or a nominee of the Depositary (we will refer to any debt security represented by a global debt security as a "book-entry debt security"), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a "certificated debt security") as set forth in the applicable prospectus supplement. Except as set forth under the heading "Global Debt Securities and Book-Entry System" below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depositary, and registered in the name of the Depositary or a nominee of the Depositary. Please see "Global Securities."

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection In the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a "successor person") unless:

- we are the surviving corporation or the successor person (if other than us) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and

immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

"Event of Default" means with respect to any series of debt securities, any of the following:

default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);

default in the payment of principal of any debt security of that series at its maturity;

default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Hemispherx and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;

certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Hemispherx; or

any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain of our indebtedness or that of our subsidiaries outstanding from time to time.

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee will be under no obligation to exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in exercising such right of power. (Section 7.1(e)) Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and

the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered reasonable indemnity or security, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt

securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the debt securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each Securityholder of the debt securities of that series notice of a Default or Event of Default within 90 days after it occurs. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify and amend the indenture or the debt securities of any series without the consent of any holder of any debt security:

to cure any ambiguity, defect or inconsistency;

to comply with covenants in the indenture described above under the heading “Consolidation, Merger and Sale of Assets”;

to provide for uncertificated securities in addition to or in place of certificated securities;

to make any change that does not adversely affect the rights of any holder of debt securities;

to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;

to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or

to comply with requirements of the Commission in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments.

We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;

reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;

reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;

reduce the principal amount of discount securities payable upon acceleration of maturity;

waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);

make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;

make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or

waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

we may omit to comply with the covenant described under the heading “Consolidation, Merger and Sale of Assets” and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and

any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (“covenant defeasance”).

The conditions include:

depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that

issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and

delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

Covenant Defeasance and Events of Default. In the event we exercise our option to effect covenant defeasance with respect to any series of debt securities and the debt securities of that series are declared due and payable because of the occurrence of any Event of Default, the amount of money and/or U.S. government obligations or foreign government obligations on deposit with the trustee will be sufficient to pay amounts due on the debt securities of that series at the time of their stated maturity but may not be sufficient to pay amounts due on the debt securities of that series at the time of the acceleration resulting from the Event of Default. However, we shall remain liable for those payments. (Section 8.4).

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York without regard to conflict of law principles that would result in the application of any law other than the laws of the State of New York. (Section 10.10)

DESCRIPTION OF COMMON STOCK

The following summary of the terms of our common stock does not purport to be complete and is subject to and qualified in its entirety by reference to our Amended and Restated Certificate of Incorporation as subsequently amended, or certificate of incorporation, and Amended and Restated Bylaws, or bylaws, copies of which are on file with the Commission as exhibits to registration statements previously filed by us. See "Where You Can Find More Information."

General

Our authorized capital stock currently consists of 350,000,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of preferred stock, $0.01 par value per share. As of June 1, 2015, we had 242,554,673 shares of common stock outstanding; an aggregate of 16,905,280 shares of common stock reserved for issuance upon exercise of outstanding stock options and warrants; and an aggregate of 687,543 shares of common stock reserved for issuance pursuant to future grants under our 2009 Equity Incentive Plan. As of June 1, 2015, we had approximately 660,684 shares of common stock that are not reserved for issuance or subject to restrictions (see "Limitations on Use" below).

The following summary of the rights of our common stock is not complete and is qualified in its entirety by reference to our amended and restated certificate of incorporation, as subsequently amended, and amended and restated bylaws, copies of which are filed as exhibits to the registration statement of which this prospectus is a part.

Limitations on Use

Pursuant to our Certificate of Incorporation, there are specific limitations and restrictions on our ability to issue 150,000,000 of the 350,000,000 authorized shares of common stock, unless such issuances are primarily in connection

with strategic transactions or other non-fundraising purpose that met certain significant criteria. If we want to issue any of these shares for other purposes, we must first seek stockholder approval. In September 2012, our stockholders authorized our Board to use 75,000,000 of the 150,000,000 shares for fundraising purposes.

Voting Rights

Holders of our common stock are entitled to one vote per share on all matters to be voted upon by the stockholders. The holders of common stock are not entitled to cumulate voting rights with respect to the election of directors, which means that the holders of a majority of the shares voted can elect all of the directors then standing for election.

Dividends

Subject to limitations under Delaware law and preferences that may apply to any outstanding shares of preferred stock, holders of our common stock are entitled to receive ratably such dividends or other distribution, if any, as may be declared by our board of directors out of funds legally available therefor.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to the liquidation preference of any outstanding preferred stock.

Rights and Preferences

The common stock has no preemptive, conversion or other rights to subscribe for additional securities. There are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Fully Paid and Nonassessable

All outstanding shares of our common stock are, and all shares of common stock to be outstanding upon completion of the offering will be, validly issued, fully paid and nonassessable.

Certificate of Incorporation and Bylaw Provisions

See “Certain Provisions of Delaware Law and of the Company’s Certificate of Incorporation and Bylaws” for a description of provisions of our certificate of incorporation and bylaws which may have the effect of delaying changes in our control or management.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company.

DESCRIPTION OF PREFERRED STOCK

We currently have authorized 5,000,000 shares of preferred stock, $0.01 par value per share. As of the date of this prospectus, we did not have any shares of preferred stock outstanding.

General

Prior to issuance of shares of each series of our undesignated preferred stock, our board of directors is required by the Delaware General Corporate Law, or DGCL, and our Amended and Restated Certificate of Incorporation as subsequently amended, or certificate of incorporation, to adopt resolutions and file a Certificate of Designations with the Secretary of State of the State of Delaware, fixing for each such series the designations, powers, preferences, rights, qualifications, limitations and restrictions of the shares of such series. Our board of directors could authorize the issuance of shares of preferred stock with terms and conditions which could have the effect of discouraging a takeover or other transaction which holders of some, or a majority, of such shares might believe to be in their best interests or in which holders of some, or a majority, of such shares might receive a premium for their shares over the then-market price of such shares.

Subject to limitations prescribed by the DGCL, our certificate of incorporation and our Amended and Restated Bylaws, or bylaws, our board of directors is authorized to fix the number of shares constituting each series of preferred stock and the designations, powers, preferences, rights, qualifications, limitations and restrictions of the shares of such series, including such provisions as may be desired concerning voting, redemption, dividends,

dissolution or the distribution of assets, conversion or exchange, and such other subjects or matters as may be fixed by resolution of the board of directors. Each series of preferred stock that we offer under this prospectus will, when issued, be fully paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

The applicable prospectus supplement(s) will describe the following terms of the series of preferred stock in respect of which this prospectus is being delivered:

- the title and stated value of the preferred stock;
- the number of shares of the preferred stock offered, the liquidation preference per share and the purchase price of the preferred stock;
- the dividend rate(s), period(s) and/or payment date(s) or the method(s) of calculation for dividends;
- whether dividends shall be cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock shall accumulate;
- the procedures for any auction and remarketing, if any, for the preferred stock;
- the provisions for a sinking fund, if any, for the preferred stock;
- the provisions for redemption, if applicable, of the preferred stock;
- any listing of the preferred stock on any securities exchange or market;
- the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock or another series of our preferred stock, including the conversion price (or its manner of calculation) and conversion period;
- the terms and conditions, if applicable, upon which preferred stock will be exchangeable into our debt securities, including the exchange price, or its manner of calculation, and exchange period;
- voting rights, if any, of the preferred stock;

- a discussion of any material and/or special U.S. federal income tax considerations applicable to the preferred stock;
- whether interests in the preferred stock will be represented by depositary shares;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs;
- any limitations on issuance of any series of preferred stock ranking senior to or on a parity with the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and
- any other specific terms, preferences, rights, limitations or restrictions on the preferred stock.

Rank

Unless otherwise specified in the prospectus supplement, with respect to dividend rights and rights upon liquidation, dissolution or winding up of Hemispherx, the preferred stock will rank:

- senior to all classes or series of our common stock, and to all equity securities issued by us the terms of which specifically provide that such equity securities rank junior to the preferred stock with respect to dividend rights or rights upon the liquidation, dissolution or winding up of us;
- on a parity with all equity securities issued by us that do not rank senior or junior to the preferred stock with respect to dividend rights or rights upon the liquidation, dissolution or winding up of us; and
- junior to all equity securities issued by us the terms of which do not specifically provide that such equity securities rank on a parity with or junior to the preferred stock with respect to dividend rights or rights upon the liquidation, dissolution or winding up of us (including any entity with which we may be merged or consolidated or to which all or substantially all of our assets may be transferred or which transfers all or substantially all of our assets).

As used for these purposes, the term “equity securities” does not include convertible debt securities.

Transfer Agent and Registrar

The transfer agent and registrar for any series or class of preferred stock will be set forth in the applicable prospectus supplement.

DESCRIPTION OF WARRANTS

We may issue debt warrants to purchase debt securities, as well as equity warrants to purchase common stock or preferred stock. The warrants may be issued independently or together with any securities and may be attached to or separate from the securities. The warrants may be issued directly by us or under warrant agreements to be entered into between us and a bank or trust company, as warrant agent, all as shall be set forth in the prospectus supplement relating to warrants being offered pursuant to such prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

Debt Warrants

The applicable prospectus supplement will describe the terms of debt warrants offered, the warrant agreement relating to the debt warrants and the debt warrant certificates representing the debt warrants, including the following:

- the title of the debt warrants;
- the aggregate number of the debt warrants;
- the price or prices at which the debt warrants will be issued;

the designation, aggregate principal amount and terms of the debt securities purchasable upon exercise of the debt warrants, and the procedures and conditions relating to the exercise of the debt warrants;

the designation and terms of any related debt securities with which the debt warrants are issued, and the number of debt warrants issued with each debt security;

the date, if any, on and after which the debt warrants and the related debt securities will be separately transferable;

the principal amount of debt securities purchasable upon exercise of each debt warrant;

the date on which the right to exercise the debt warrants will commence, and the date on which this right will expire;

the maximum or minimum number of debt warrants which may be exercised at any time;

a discussion of any material Federal income tax considerations; and

any other terms of the debt warrants and terms, procedures and limitations relating to the exercise of debt warrants.

Debt warrants may be exercised at the corporate trust office of the warrant agent or any other office indicated in the prospectus supplement. Prior to the exercise of their debt warrants, holders of debt warrants will not have any of the rights of holders of the debt securities purchasable upon exercise and will not be entitled to payment of principal or any premium, if any, or interest on the debt securities purchasable upon exercise.

Equity Warrants

The applicable prospectus supplement will describe the following terms of equity warrants offered:

the title of the equity warrants;

the securities (i.e., common stock or preferred stock) for which the equity warrants are exercisable;

the price or prices at which the equity warrants will be issued;

if applicable, the designation and terms of the common stock or preferred stock with which the equity warrants are issued, and the number of equity warrants issued with each share of common stock or preferred stock;

if applicable, the date on and after which the equity warrants and the related common stock or preferred stock will be separately transferable;

if applicable, a discussion of any material Federal income tax considerations; and

any other terms of the equity warrants, including terms, procedures and limitations relating to the exchange and exercise of equity warrants.

Prior to exercise of the equity warrants, holders of equity warrants will not be entitled, by virtue of being such holders, to vote, consent, receive dividends, receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter, or to exercise any rights whatsoever as our stockholders.

The exercise price payable and the number of shares of common stock or preferred stock purchasable upon the exercise of each equity warrant will be subject to adjustment in certain events, including the issuance of a stock dividend to holders of common stock or preferred stock or a stock split, reverse stock split, combination, subdivision or reclassification of common stock or preferred stock. In lieu of adjusting the number of shares of common stock or preferred stock purchasable upon exercise of each equity warrant, we may elect to adjust the number of equity warrants. No adjustments in the number of shares purchasable upon exercise of the equity warrants will be required until cumulative adjustments require an adjustment of at least 1% thereof. We may, at our option, reduce the exercise price at any time. No fractional shares will be issued upon exercise of equity warrants, but we will pay the cash value of any fractional shares otherwise issuable. Notwithstanding the foregoing, in case of any consolidation, merger, or sale or conveyance of our property in its entirety or substantially in its entirety, the holder of each outstanding equity warrant shall have the right to the kind and amount of shares of stock and other securities and property, including cash, receivable by a holder of the number of shares of common stock or preferred stock into which the equity warrant was exercisable immediately prior to such transaction.

Exercise of Warrants

Each warrant will entitle the holder to purchase for cash such principal amount of securities or shares of stock at such exercise price as shall in each case be set forth in, or be determinable as set forth in, the prospectus supplement relating to the warrants offered thereby. Warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the securities purchasable upon such exercise. If less than all of the warrants represented by such warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

DESCRIPTION OF UNITS

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. We may issue units consisting of two or more other constituent securities. These units may be issuable as, and for a specified period of time may be transferable only as a single security, rather than as the separate constituent securities comprising such units. While the features we have summarized below will generally apply to any units we may offer under this prospectus, we will describe the particular terms of any units that we may offer in more detail in the applicable prospectus supplement. The specific terms of any units may differ from the description provided below as a result of negotiations with third parties in connection with the issuance of those units, as well as for other reasons. Because the terms of any units we offer under a prospectus supplement may differ from the terms we describe below, you should rely solely on information in the applicable prospectus supplement if that summary is different from the summary in this prospectus.

We urge you to read the applicable prospectus supplement related to the specific units being offered, as well as the complete instruments that contain the terms of the securities that comprise those units. Certain of those instruments, or forms of those instruments, have been or will be filed as exhibits to the registration statement of which this prospectus is a part, and supplements to those instruments or forms may be incorporated by reference into the registration statement of which this prospectus is a part from reports we file with the Commission.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in a prospectus supplement, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depositary, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depositary to its nominee or by the nominee to the depositary, or by the depositary or its nominee to a successor depositary or to a nominee of the successor depositary.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law,
- a "banking organization" within the meaning of the New York Banking Law,
- a member of the Federal Reserve System,
- a "clearing corporation" within the meaning of the New York Uniform Commercial Code, and
- a "clearing agency" registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds and provides asset servicing for issues of U.S. and non-U.S. equity issues, corporate and municipal debt issues, and money market instruments from many countries that its participants ("Direct Participants") deposit with it. DTC also facilitates the post-trade settlement among Direct Participants of sales and other securities transactions in deposited securities, through electronic computerized book-entry transfers and pledges between Direct Participants' accounts. This eliminates the need for physical movement of securities certificates. Direct Participants include both U.S. and non-U.S. securities brokers and dealers, banks, trust companies, clearing corporations, and certain other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation ("DTCC"). DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others such as both U.S. and non-U.S. securities brokers and dealers, banks, trust companies, and clearing corporations that clear through or maintain a custodial relationship with a Direct Participant, either directly or indirectly ("Indirect Participants"). The DTC Rules applicable to its Participants are on file with the Securities and Exchange Commission.

Purchases of securities under the DTC system must be made by or through Direct Participants, which will receive a credit for the securities on DTC's records. The ownership interest of each actual purchaser of each security ("Beneficial Owner") is in turn to be recorded on the Direct and Indirect Participants' records. Beneficial Owners will not receive written confirmation from DTC of their purchase. Beneficial Owners are, however, expected to receive written confirmations providing details of the transaction, as well as periodic statements of their holdings, from the Direct or Indirect Participant through which the Beneficial Owner entered into the transaction. Transfers of ownership interests in the securities are to be accomplished by entries made on the books of Direct and Indirect Participants acting on behalf of Beneficial Owners. Beneficial Owners will not receive certificates representing their ownership interests in securities, except in the event that use of the book-entry system for the securities is discontinued.

To facilitate subsequent transfers, all global securities deposited by Direct Participants with DTC will be registered in the name of DTC's partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other DTC nominee will not effect any change in beneficial ownership. DTC has no knowledge of the actual

Beneficial Owners of the securities; DTC's records reflect only the identity of the Direct Participants to whose accounts such securities are credited, which may or may not be the Beneficial Owners. The Direct and Indirect Participants will be responsible for keeping account of their holdings on behalf of their customers.

Conveyance of notices and other communications by DTC to Direct Participants, by Direct Participants to Indirect Participants, and by Direct Participants and Indirect Participants to Beneficial Owners will be governed by arrangements among them, subject to any statutory or regulatory requirements as may be in effect from time to time. Beneficial Owners of securities may wish to take certain steps to augment the transmission to them of notices of significant events with respect to the securities, such as redemptions, tenders, defaults, and proposed amendments to the security documents. For example, Beneficial Owners of securities may wish to ascertain that the nominee holding the securities for their benefit has agreed to obtain and transmit notices to Beneficial Owners. In the alternative, Beneficial Owners may wish to provide their names and addresses to the registrar and request that copies of notices be provided directly to them.

Redemption notices will be sent to DTC. If less than all of the Securities within an issue are being redeemed, DTC's practice is to determine by lot the amount of the interest of each Direct Participant in such issue to be redeemed.

Neither DTC nor Cede & Co. (nor any other DTC nominee) will consent or vote with respect to Securities unless authorized by a Direct Participant in accordance with DTC's MMI Procedures. Under its usual procedures, DTC mails an Omnibus Proxy to us as soon as possible after the record date. The Omnibus Proxy assigns Cede & Co.'s consenting or voting rights to those Direct Participants to whose accounts Securities are credited on the record date, as identified in a listing attached to the Omnibus Proxy.

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depositary and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Redemption proceeds, distributions, and dividend payments on the Securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit Direct Participants' accounts upon DTC's receipt of funds and corresponding detail information from us, on payable date in accordance with their respective holdings shown on DTC's records. Payments by Participants to Beneficial Owners will be governed by standing instructions and customary practices, as is the case with securities held for the accounts of customers in bearer form or registered in "street name," and will be the responsibility of such Participant and not of DTC, or us, subject to any statutory or regulatory requirements as may be in effect from time to time. Payment of redemption proceeds, distributions, and dividend payments to Cede & Co. (or such other nominee as may be requested by an authorized representative of DTC) is our responsibility, disbursement of such payments to Direct Participants will be the responsibility of DTC, and disbursement of such payments to the Beneficial Owners will be the responsibility of Direct and Indirect Participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained, security certificates are required to be printed and delivered.

As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

DTC notifies us that it is unwilling or unable to continue as a depositary for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depositary is not appointed within 90 days of the

notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;

we determine, in our sole discretion, not to have such securities represented by one or more global securities; or

an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depositary directs. It is expected that these directions will be based upon directions received by the depositary from its participants with respect to ownership of beneficial interests in the global securities.

We have obtained the information in this section and elsewhere in this prospectus concerning DTC and DTC's book-entry system from sources that are believed to be reliable, but we take no responsibility for the accuracy of this information.

CERTAIN PROVISIONS OF DELAWARE LAW AND OF THE

COMPANY'S CERTIFICATE OF INCORPORATION AND BYLAWS

Delaware Takeover Statute

We are subject to Section 203 of the DGCL. This statute regulating corporate takeovers prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for three years following the date that the stockholder became an interested stockholder, unless:

prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (a) shares owned by persons who are directors and also officers and (b) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

Subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Certificate of Incorporation and Bylaw Provisions

Provisions of our certificate of incorporation and bylaws may have the effect of making it more difficult for a third party to acquire, or discourage a third party from attempting to acquire, control of our company by means of a tender offer, a proxy contest or otherwise. These provisions may also make the removal of incumbent officers and directors more difficult. These provisions are intended to discourage certain types of coercive takeover practices and inadequate takeover bids and to encourage persons seeking to acquire control of Hemispherx to first negotiate with us. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock. These provisions may make it more difficult for stockholders to take specific corporate actions and could have the effect of delaying or preventing a change in our control.

In particular, our certificate of incorporation and bylaws, as currently amended, provide for the following:

Advance Notice Requirement

Stockholder proposals to be brought before an annual meeting of our stockholders must comply with advance notice procedures. These advance notice procedures require timely notice and apply in several situations, including stockholder proposals relating to the nominations of persons for election to the board of directors. Generally, to be timely, notice must be received at our principal executive offices not less than 60 days nor more than 90 days prior to the first anniversary date of the annual meeting for the preceding year, or where a Stockholder Proposal relates to nomination of candidates for director, not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year.

Issuance of Undesignated Preferred Stock

Our board of directors is authorized to issue, without further action by the stockholders, up to 5,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by the board of directors. As of the date of this prospectus, we have no shares of preferred stock designated or outstanding. The existence of authorized but unissued shares of preferred stock enables our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.

Limitation of Liability and Indemnification of Officers and Directors

As permitted by Section 102 of the DGCL, we have adopted provisions in our certificate of incorporation and bylaws that limit or eliminate the personal liability of our directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, directors exercise an informed business judgment based on all material information reasonably available to them. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any act related to unlawful stock repurchases, redemptions or other distributions or payment of dividends; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not affect the availability of equitable remedies such as injunctive relief or rescission. Our certificate of incorporation also authorizes us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

As permitted by Section 145 of the DGCL, our bylaws provide that:

- we may indemnify our directors, officers, employees and agents to the fullest extent permitted by the DGCL, subject to limited exceptions;
- we may advance expenses to our directors, officers, employees and agents in connection with a legal proceeding to the fullest extent permitted by the DGCL, subject to limited exceptions; and
- the rights provided in our bylaws are not exclusive.

We have purchased a policy of directors' and officers' liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment in some circumstances.

LEGAL MATTERS

Silverman Shin Byrne & Gilchrest PLLC will issue an opinion about certain legal matters with respect to the securities.

EXPERTS

The consolidated financial statements of Hemispherx Biopharma, Inc. included in the Company's Annual Report (Form 10-K) as of December 31, 2014 and 2013 and for the years then ended being incorporated by reference in this Prospectus and Registration Statement have been audited by McGladrey LLP, an independent registered public accounting firm, as stated in their report, included therein, and being incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report and upon the authority of such firm as experts in accounting and auditing.

LIMITATION ON LIABILITY AND DISCLOSURE OF COMMISSION POSITION ON

INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Our certificate of incorporation and bylaws provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by the DGCL. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the Commission, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Commission a registration statement on Form S-3 under the Securities Act, of which this prospectus forms a part. The rules and regulations of the Commission allow us to omit from this prospectus certain information included in the registration statement. For further information about us and our securities, you should refer to the registration statement and the exhibits and schedules filed with the registration statement. With respect to the statements contained in this prospectus regarding the contents of any agreement or any other document, in each instance, the statement is qualified in all respects by the complete text of the agreement or document, a copy of which has been filed as an exhibit to the registration statement.

We file reports, proxy statements and other information with the Commission under the Exchange Act. You may read and copy this information from the Public Reference Room of the Commission, 100 F Street, N.E., Room 1580, Washington, D.C. 20549, at prescribed rates. You may obtain information on the operation of the Public Reference Room by calling the Commission at 1-800-SEC-0330. The Commission also maintains an Internet website that contains reports, proxy statements and other information about issuers, like us, that file electronically with the Commission. The address of that website is *www.sec.gov*.

We also maintain a website at *www.hemispherx.net* through which you can access our filings with the Commission. The information contained in, or accessible through, our website is not a part of this prospectus.

INFORMATION INCORPORATED BY REFERENCE

The Commission allows us to "incorporate by reference" the information we file with it which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the Commission will automatically update and supersede this information. We incorporate by reference the documents listed below and any future information filed (rather than furnished) with the Commission under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this prospectus and the termination of the offering and also between the date of the initial registration statement and prior to effectiveness of the registration statement, provided, however, that we are not incorporating any information furnished under any of Item 2.02 or Item 7.01 of any current report on Form 8-K:

- our annual report on Form 10-K for the year ended December 31, 2014;
- our quarterly report on Form 10-Q for the quarter ended March 31, 2015;

our current report on Form 8-K filed with the Commission on June 24, 2015;

our preliminary proxy statement on Schedule 14A filed on July 7, 2015; and

A description of our common stock contained in our registration statement on Form S-1, SEC File No. 333-117178, and any amendment or report filed for the purpose of updating this description.

These documents may also be accessed on our website at *www.hemispherx.net*. Except as otherwise specifically incorporated by reference in this prospectus, information contained in, or accessible through, our website is not a part of this prospectus.

We will furnish without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents by writing or telephoning us at the following address:

Hemispherx Biopharma, Inc.

1617 JFK Boulevard, Ste. 500

Philadelphia, Pennsylvania 19103

Attention: Corporate Secretary

(215) 988-0800

HEMISPHERX BIOPHARMA, INC.

$77,849,014

Common Stock

Preferred Stock

Warrants

Debt Securities

PROSPECTUS

August 4, 2015

HEMISPHERX BIOPHARMA, INC.

$1,599,821

Common Stock

PROSPECTUS SUPPLEMENT

November 27, 2017

Maxim Group LLC